

Claims

1. Method of producing a product protein, wherein the protein is expressed from a
5 mammalian cell, preferably from a lymphoid cell, in cell culture at least during a
certain span of time during cell culture, comprising the steps
- e) preparing a cell culture medium for culturing mammalian cells, preferably
preparing a cell culture medium that is devoid of butyrate, and further preferred
preparing a cell culture medium allowing for growth of the mammalian cells, more
10 preferably a protein-free cell culture growth medium,
- f) and further adding acetic acid or an acetate salt or an acetyl ester to a final
concentration of from 1 to 20 mM, preferably of from 3 to 15 mM, more preferably
of from 5 to 12 mM, most preferably of from 6 to 9.5 mM, said addition being
15 carried out either directly to the medium prior to starting cell culture or feeding it to
the medium during cell culture,
- g) further culturing, preferably growing, said cell in said medium with concomittant
expression of product protein,
- h) and finally harvesting said protein from the cell culture.
- 20 2. Method according to claim 1, characterised in the the addition of acetic acid or a salt
thereof is carried out directly to the medium prior to or at starting the cell culture.
3. Method according to one of the preceding claims, characterised in that an acetate alkali
metal or alkaline earth metal salt is added to the medium.
- 25 4. Method according to one of the preceding claims, characterised in that the cells are
lymphoid cells, preferably NS0 cells.
5. Method according to claim 4, characterised in the cells are NS0 cells that are
30 recombinant for and can express Glutamine synthetase.
6. Cell culture medium for animal cell culture, characterised in that the medium is suited
for culturing mammalian cells and comprises acetic acid or an acetate salt or a

biologically activated acetyl ester at a concentration of from 1 to 20 mM, preferably of from 3 to 15 mM, more preferably of from 5 to 12 mM, most preferably at about 6 to 9.5 mM, and preferably is devoid of butyric acid or any of its salts.

- 5 7. Cell culture medium according to claim 3, characterised in that the medium is a high density cell culture medium.
8. Cell culture medium according to claim 6 or 7, characterised in that the medium is a cell culture medium allowing of growth of animal cells, preferably lymphoid cells.
- 10 9. Cell culture medium according to claims 6-8, characterised in that the medium is a serum-free and protein-free cell culture medium, preferably a protein-free medium suitable for NS0 cell culture.
- 15 10. A medium concentrate for preparation of a culture medium as defined in claim 6 which is either a solid or a liquid.
11. Use of a cell culture medium according to claim 6 for lymphoid cell culture.
- 20 12. Cell culture, comprising mammalian cells, preferably lymphoid cells, most preferably NS0 cells, in a medium according to claim 6.